

Appln. No. 09/587,662
Amendment dated December 23, 2003
Reply to Final Office Action of July 7, 2003

The listing of claims will replace all prior versions and listing of claims in the application:

Listing of Claims:

Claim 1. (Currently amended) A method for inhibiting or reducing the growth of a cell, comprising: administering a dose of a telomere damage-inducing agent being one or more of antimicrotubules, DNA alkylators, topoisomerase inhibitors or antimetabolites to the cell wherein such agent causes one or more of damaged or shortened telomeres within 24 hours or prior to the initiation of the apoptosis cascade, or ~~causes~~ telomere damage followed by a transient increase in telomerase activity; and administering a dose of telomerase inhibitory agent to the cell, such that an inhibition or reduction in the growth of the cell is achieved.

Claim 2. (canceled)

Claim 3. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said growth is aberrant.

Claim 4. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said cell is a tumor cell.

Claim 5. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said cell is a leukemia cell.

Claim 6. (Currently amended) The method of claim 4, wherein said tumor cell is one or more of the brain, breast, ovary, testes, bladder, prostate, colon, lung, liver, pancreas, or uterus.

Claim 7. (Original) The method of claim 4, wherein said tumor cell is benign.

Claim 8. (Original) The method of claim 4, wherein said tumor cell is malignant.

Claim 9. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said growth is selected from the group consisting of hyperplastic and or hypertrophic.

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- Claim 10. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said inhibition or reduction in the growth of the cell comprises apoptosis.
- Claim 11. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered serially.
- Claim 12. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered concurrently.
- Claim 13. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered in any order.
- Claim 14. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered as a timed-release formulation.
- Claim 15. (Original) The method of claim 14, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered as a timed-release formulation.
- Claim 16. (Currently amended) The method ~~any one of claims 1 or 2~~, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered locally.
- Claim 17. (Original) The method of claim 16, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered locally.
- Claim 18. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered systemically.
- Claim 19. (Original) The method of claim 18, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered systemically.
- Claim 20. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered regionally.

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Claim 21. (Original) The method of claim 20, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered systemically.

Claim 22. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said cell is in a human.

Claim 23. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof.

Claim 24. (Currently amended) The method of ~~any one of claims 1 or 2~~, wherein said telomerase inhibitory agent is a nucleoside analog, or derivative thereof.

Claim 25. (Cancelled)

Claim 26. (Previously amended) The method of claim 24, wherein said nucleoside analog is AZT in a dose of no more than about 0.24 mg/kg/day.

Claim 27. (Previously amended) The method of claim 24, wherein said nucleoside analog is d4T in a concentration of at least about 20 micromolar.

Claim 28. (Currently amended) The method of any one of claims 1 ~~or 2~~, wherein said agent selected from the group consisting of telomere damage-inducing agent and telomerase inhibitory agent, is administered as a subtherapeutic dose.

Claims 29-32 (Cancelled).

Claim 33 (Currently amended). A method of screening a candidate agent effective for inhibiting or reducing the growth of an aberrant cell and for treating a patient with said screened candidate agent comprising:
contacting an aberrant cell with at least one agent and determining if telomere damage has occurred;
contacting an aberrant with the same or at least one other agent and determining if a reduction in telomerase activity has occurred, whereby an agent or agents, alone or in combination, that are determined to induce telomere damage and inhibit telomerase

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activity, are indicated as an agent or agents that inhibits or reduces the growth of a cell;
and
administering to a ~~cell~~ patient a therapeutically effective amount of the identified agent or agents.

Claim 34 (Currently amended). A method of screening an agent for treating aberrant cell growth in a mammal comprising:
contacting an aberrant cell with at least one agent a telomere damage-inducing agent being one or more of antimicrotubules, DNA alkylators, topoisomerase inhibitors or antimetabolites and determining if telomere damage has occurred;
contacting an aberrant cell with the same or at least one other agent and determining if a reduction in telomerase activity has occurred, whereby an agent or agents, alone or in combination, that are determined to induce telomere damage and inhibit telomerase activity, are indicated as an agent or agents that inhibits or reduces the growth of a cell;
and
administering to a mammal a therapeutically effective amount of the identified agent or agents.

Claim 35 (Original). The method of claim 34 wherein said mammal is a human.

Claims 36-39 (Cancelled).

Claim 40. (Canceled)

Claim 41 (Canceled)

Claim 42. (Currently amended) A method of treating cancer in a patient comprising,
~~obtaining an agent selected from the group consisting of a telomere damage-inducing agent~~ a telomere damage-inducing agent being one or more of antimicrotubules, DNA alkylators, topoisomerase inhibitors or antimetabolites to said patient wherein such agent causes one or more of damaged or shortened telomeres within 24 hours or prior to the initiation of the apoptosis cascade, or causes telomere damage followed by a transient increase in telomerase activity, and a telomerase inhibitory agent;
administering a therapeutically-effective amount of said telomere damage-inducing agent to said patient; and

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administering a therapeutically-effective amount of a telomerase inhibitory agent to said patient, such that treatment of the cancer is achieved.

Claim 43 (Previously amended). The method of claim 42, wherein the method further comprises identifying a patient having cancer.

Claim 44 (Currently amended). The method of ~~any one of claims 40 or~~ 42, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof.

Claim 45. (Currently amended) The method of ~~any one of claims 40 or~~ 42, wherein said telomerase inhibitory agent is a nucleoside analog, or derivative thereof.

Claim 46. (Previously amended) The method of claim 45, wherein said nucleoside analog is AZT.

Claim 47. (Previously amended) The method of claim 45, wherein said nucleoside analog is d4T.

Claims 48-89 (Cancelled).

Claim 90 (Previously added). The method of claim 24, wherein said nucleoside analog is d4T in a dose that produces at least about 20 micromolar plasma concentration in a subject.

Claim 91 (Currently amended). The method of ~~any one of claims~~ claim 26, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof, and the ratio of the AZT concentration to the telomere damage-inducing agent concentration is about 40:60 of their respective therapeutic concentrations.

Claim 92 (Currently amended). The method of ~~any one of claims~~ claim 26, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof, and the ratio of the AZT concentration to the telomere damage-inducing agent concentration is about 40:60 of their respective therapeutic doses.

Claim 93 (New) The method of claim 1 wherein the telomere damage-inducing agent is an antimicrotubule.

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Claim 94 (New) The method of claim 1 wherein the telomere damage-inducing agent is a DNA alkylator.

Claim 95 (New) The method of claim 1 wherein the telomere damage-inducing agent is a topoisomerase inhibitor.

Claim 96 (New) The method of claim 1 wherein the telomere damage-inducing agent is an antimetabolite.

Claim 97. (New) A method for inhibiting or reducing the growth of a cell, comprising:
administering a dose of a telomere damage-inducing agent being one or more of paclitaxel, docetaxel, vincristine, cisplatin, doxorubicin, mitoxantrone, methotrexate, or 5-fluorouracil to the cell wherein such agent causes one or more of damaged or shortened telomeres within 24 hours or prior to the initiation of the apoptosis cascade, or telomere damage followed by a transient increase in telomerase activity; and
administering a dose of telomerase inhibitory agent to the cell, such that an inhibition or reduction in the growth of the cell is achieved.

Claim 98 (New) The method of claim 97 wherein the telomere damage-inducing agent is one or more of paclitaxel, docetaxel and vincristine.

Claim 99 (New) The method of claim 97 wherein the telomere damage-inducing agent is cisplatin.

Claim 100 (New) The method of claim 97 wherein the telomere damage-inducing agent is one or more of doxorubicin or mitoxantrone.

Claim 101 (New) The method of claim 97 wherein the telomere damage-inducing agent is one or more of methotrexate, or 5-fluorouracil.

Claim 102. (New) The method of claim 97, wherein said growth is aberrant.

Claim 103. (New) The method of claim 97, wherein said cell is a tumor cell.

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- Claim 104. (New) The method of claim 97, wherein said cell is a leukemia cell.
- Claim 105. (New) The method of claim 103, wherein said tumor cell is one or more of the brain, breast, ovary, testes, bladder, prostate, colon, lung, liver, pancreas, or uterus.
- Claim 106. (New) The method of claim 103, wherein said tumor cell is benign.
- Claim 107. (New) The method of claim 103, wherein said tumor cell is malignant.
- Claim 108. (New) The method of claim 97, wherein said growth is one or more of hyperplastic or hypertrophic.
- Claim 109. (New) The method of claim 97, wherein said inhibition or reduction in the growth of the cell comprises apoptosis.
- Claim 110. (New) The method of claim 97, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered serially.
- Claim 111. (New) The method of claim 97, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered concurrently.
- Claim 112. (New) The method of claim 97, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered in any order.
- Claim 113. (New) The method of claim 97, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered as a timed-release formulation.
- Claim 114. (New) The method of claim 113, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered as a timed-release formulation.
- Claim 115. (New) The method of claim 97, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered locally.
- Claim 116. (New) The method of claim 115, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered locally.

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Claim 117. (New) The method of claim 97, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered systemically.

Claim 118. (New) The method of claim 117, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered systemically.

Claim 119. (New) The method of claim 97, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered regionally.

Claim 120. (New) The method of claim 119, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered systemically.

Claim 121. (New) The method of claim 97, wherein said cell is in a human.

Claim 122. (New) The method of claim 97, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof.

Claim 123. (New) The method of claim 97, wherein said telomerase inhibitory agent is a nucleoside analog, or derivative thereof.

Claim 124. (New) The method of claim 123, wherein said nucleoside analog is AZT in a dose of no more than about 0.24 mg/kg/day.

Claim 125. (New) The method of claim 123, wherein said nucleoside analog is d4T in a concentration of at least about 20 micromolar.

Claim 126. (New) The method of claim of claim 97, wherein said agent is one or more of telomere damage-inducing agent and telomerase inhibitory agent, is administered as a subtherapeutic dose.